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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/716,356	11/21/2000	Shimpei Ushio	USHIO-2	8174

1444 7590 05/19/2003

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	15

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/716,356	USHIO ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-9 and 18-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,2 and 4-9* is/are allowed.

6)☒ Claim(s) *18 and 20-52* is/are rejected.

7)☒ Claim(s) *19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

1. Currently, claims 1, 2, 4-9, and 18-52 are pending and under consideration in this application. In the prior action, mailed on October 22, 2002, claims 1-9, and 18-61 were pending, under consideration, and rejected, and claims 10-17, and 62-94 were pending, and withdrawn as drawn to non-elected inventions.

2. In the Response, filed March 24, 2003, the applicant cancelled the non-elected claims 10-17, and 62-94, as well as elected claims 3, and 53-61. The applicant also amended claims 18 and 19. With the Response, the Applicant also filed a terminal disclaimer, which refers to commonly owned U.S. patents 6,214,584, 6,441,138, 6,403,079, and 6,207,641.

3. Because this action raises new issues not raised in the prior action, the rejection is being made Non-Final.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on November 21, 2000 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner, except to the extent indicated in the prior action (re: the references in foreign languages). The Examiner apparently overlooked the abstract page of the document XP 002024314 (abstract of JP 05279376) in parent application 08/832,180. The reference has now been considered.

Double Patenting

5. **(Prior Rejections- Withdrawn)** Claim 3 was rejected in the prior action under 35 U.S.C. 101 as claiming the same invention as that of claim 29 of prior U.S. Patent No. 6,214,584. Similarly, claims 53, 54, 55, 57, 58, 56, 59, 60, and 61 were rejected in that action as claiming the same invention as is claims 1-9 of prior U.S. Patent No. 6,207,641. As all of these claims have been cancelled from the application, the rejections are hereby withdrawn.

6. **(Prior Rejections-Withdrawn)** Claims 1, 2, 4, and 5 were rejected in the prior action under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27, 28, 30, and 31 of U.S. Patent No. 6,214,584 in view of claim 29 from that same patent.

Claims 1-4, 6-9 and 18, 19, 21-55, 57-61 were rejected in the prior action under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,441,138, and likewise rejected over claims 1-3 of Patent 6,403,079.

Claims 1-9, and 18-61 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,207,641. In view of the Terminal Disclaimer filed on March 24, 2003 with respect to these patents, all of the above obviousness type double patenting rejections are hereby withdrawn.

Claim Objections

7. **(Prior Objection –Withdrawn)** Claims 53, and its dependant claims 54-61, were objected to in the prior action because of the following informalities: In the listing of the physiochemical properties of the polypeptide, the claim fails to specify the biological activity required (i.e. limitation (d) is incomplete). As these claims have been cancelled from the Application, the objection is hereby withdrawn as moot.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. **(Prior Rejections- Withdrawn)** Claims 18, 20, 21-52, and 53-57 are rejected under 35 U.S.C. 112, first paragraph, both for exceeding the scope of enablement, and for lack of written description, for those parts of the claims that read on homologous sequences comprising one or more (at least one) substitutions or deletions within the sequence of SEQ ID NO: 6. The Applicant's arguments with respect to these rejections were persuasive. The rejections are therefore withdrawn.

10. **(Prior Rejection- Maintained)** Claims 18, 20, 21-52, and 53-57 were rejected in the prior action under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising SEQ ID NO: 6, or for derivatives thereof varying from SEQ ID NO: 6 by one amino acid residue, does not reasonably provide enablement for a composition

comprising any homologue of the sequence. The claims read on compositions comprising the polypeptides of SEQ ID NO: 6, or homologous sequences comprising one or more (at least one) substitutions or deletions within the sequence of SEQ ID NO: 6. In view of the cancellation of claims 53-57, the rejection is withdrawn as to these claims as moot, but maintained against the remaining claims for the reasons indicated below.

The Applicant has traversed this rejection on the grounds that the Applicant, by disclosing two sequences which may be compared, would have allowed those skilled in the art to be able to determine what residues are likely to be necessary for the protein to function, and to therefore enable them to derive protein homologues. The Applicant provided no other guidance that would lead those in the art to other operative sequences.

The Applicant's argument has not been found persuasive. While the Applicant has shown two samples of IGIF sequences, the Applicant has not shown that these are representative of all IGIF sequences. Further, the Applicant has not identified what residues or regions of the disclosed IGIF sequence are necessary for protein function. While comparison of the sequences may provide some guidance, absent more one skilled in the art would not know which of the conserved regions are necessary to protein function. For example, in a sequence alignment, the sequences of SEQ ID NOs: 4 and 6 share a 60% homology. In the alignment of the sequences, one of the more closely related sequence regions comprises residues 97-113. This region has 2 conservative substitutions (Ile99Leu, Arg104Lys), one non-conservative substitution (Ser105Arg), and one deletion (Asp110). Absent further information, one in the art may have felt that this sequence was likely to be necessary to protein function. However, an IGIF homologue, and an isoform thereof lacking this region, have been described in the art. See, Joh et al., WO

98/10072, pages 6-8. Thus, what one of ordinary skill in the art may have recognized as necessary for protein function from the presently disclosed sequences was unpredictably disclosed as unnecessary. This demonstrates that the Applicant has not provided sufficient information about the claimed genus of IGIF proteins for one skilled in the art to make or use homologues of SEQ ID NO: 6 because such a person would not know from the present disclosure what residues are and are not available for manipulation.

11. **(Prior Rejection-Maintained)** Claims 18, 20, 21-52, and 53-57 were rejected in the prior action under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims were rejected because the Application does not provide adequate support for claims to the genus of all homologues to the interferon-gamma inducing factor (IGIF) of SEQ ID NO: 6. In view of the cancellation of claims 53-57, the rejection is withdrawn as to these claims as moot, but maintained against the remaining claims for the reasons indicated below.

The Applicant has traversed this rejection on the grounds that the Applicant has disclosed two sample of IGIF, and that one of ordinary skill in the art would be able to determine from a comparison of the sequences what residues were likely to be important to protein function. The Examiner disagrees. The Applicant has described homologues as encompassing variants with any number (one or more) of substitutions, or C- or N-terminal additions or deletions, so long as the protein maintains the "inherent biological activity of the present IFN-γ inducing polypeptide." App., page 9, lines 16-23. Thus, the Applicant has defined the

homologues of SEQ ID NO: 6 by their ability to retain the function of the disclosed protein. Thus, as was indicated in the prior action, the Applicant must disclose sufficient information such that one skilled in the art would recognize that the applicant was in possession of all such proteins with the ability to induce interferon-γ production.

The Applicant argues that they have provided such information through the disclosure of SEQ ID NOs: 4 and 6. The Applicant argues that from these two sequences, those in the art would be able to determine which residues were necessary for the claimed activity, and thus be able to determine what proteins fall within the claimed genus. Although the two sequences do show approximately 60% homology, the Examiner does not agree that it is apparent from a comparison between the sequences which residues are, and are not, necessary to function as there does not appear to any area of concentrated homology between the sequences. Further, while the Applicant has argued that one of ordinary skill in the art would recognize from these two sequences which sequences are likely to be necessary for function, provided the same two sequences, the Applicant has not identified any residues that would be necessary for protein function. Absent either a clear demonstration of what is needed for a functional protein, or a disclosure of the characteristics required for the performance of the function, the Applicant cannot be said to be in possession of the claimed genus of IGIF proteins.

Because the Applicant cannot be said to have been in possession of all homologues to the protein of SEQ ID NO: 6, and because the two sequences disclosed by the Applicant are not sufficient to identify all members of the claimed genus, the Applicant has not provided an adequate written description of the claimed genus.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. **(Prior Rejection-Withdrawn)** Claims 18, 20, 21-52, 57, and 53-57 were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims read on embodiments of the claimed invention wherein the composition comprises a homologue of SEQ ID NO: 6 comprising at least one substitutions or deletions. The Applicant's traversal is noted, as is the description of homologous variants on page 9 of the Application, describing such proteins as any protein with any number (one or more) of substitutions, or C- or N-terminal additions or deletions, to the sequence of SEQ ID NO: 6, so long as the functionality of the disclosed protein is maintained. Absent further specificity from the Applicant, this definition is accepted for the term homologue, and the rejection is withdrawn.

14. **(Prior Rejection- Withdrawn)** Claim19 was rejected in the prior action 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of amendments to the claim, and the Applicants argument in traversal of the rejection, the rejection is hereby withdrawn.

15. **(Prior Rejection-Withdrawn)** Claims 53 and its dependant claims 54-61, were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention. In view of the cancellation of these claims from the application, the rejection is withdrawn.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

17. **(Prior Rejection-Withdrawn)** Claims 53, 56, 57, and 60 were rejected in the prior action under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,912,324, issued to Okamura et al. These claims have been cancelled from the application. In view of this cancellation, the rejection is hereby withdrawn.

18. **(New Rejection)** Claims 18, 20, 21, 24, 27, and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,912,324, issued to Okamura et al. These claims read on homologues of SEQ ID NO: 6 having the properties of having a molecular weight of 18,500 ± 3,000 daltons, an isoelectric point of 4.9±1.0 on chromatofocusing, and a biological activity of inducing interferon-γ production. Okamura also teaches an interferon-γ inducing polypeptide. As is demonstrated by claim 1 of the patent, the polypeptide disclosed therein has a similar

molecular weight and isoelectric point with the currently claimed polypeptide. Further, in column 7 of the patent, the polypeptide is disclosed as being usable with interleukin-2 an/or with a tumor necrosis factor. Thus, the reference anticipates that stated claims.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

19. **(New Rejection)** Claims 18, and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Joh et al., WO 98/10072. This reference teaches homologues of SEQ ID NO: 6, that such homologues may be combined with suitable carriers, and be administered to animals to induce immune responses. Pages 5-8,15, and 22. Because the Applicant has not provided adequate support for the claimed genus of homologues, and because the Applicant has not taught the homologue disclosed by the reference in the priority documents, this reference is applicable as prior art against the identified claims.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. **(New Rejection)** Claims 21-23, 25, 26, and 28-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Number 5,912,324, issued to Okamura et al., as applied against claims 18, 20, 21, 24, 27, and 28 above. The rejected claims identify various compounds that may be combined with the claimed IGIF homologue in pharmaceutical compositions. IGIF is disclosed in the reference as useful for the treatment of various disorders and diseases (Okamura: column 2 lines 9-13, and column 6 lines 54-61, column 7, lines 33-39, and column 26 lines 35-49). Further, in teaching that the protein may be combined with interleukin-2 or TNF (column 7, lines 33-39), the reference indicates that the protein is effective when combined with other drugs effective in such treatments. As the compounds listed in the rejected claims were also known to be useful for the treatment of one or more of these disorders or diseases, it would have been obvious to one of ordinary skill in the art to have combined the claimed homologue with any one of them.

22. **(New Rejection)** Claims 18, 20, 21, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhou et al. (J Immunol 155:785-795), in view of Okamura et al. (Nature 378:88-91). These claims read on pharmaceutical compositions of interleukin-12 (IL-12) and homologues of the IGIF of SEQ ID NO: 6. Zhou teaches the inhibition of infection of mice by a

fungus through inducing T-cell responses by administering IL-12. Abstract. Pages 785-86. The reference teaches that IL-12's ability to induce IFN-γ was the reason the cytokine was effective in treating infected animals. Page 785. However, the reference does not teach the use of a composition comprising both an IGIF and IL-12.

Okamura teaches a homologue to the IGIF of SEQ ID NO: 6. Page 89. The reference also teaches that this homologue was able to synergistically induce the expression of INF-γ in mice when administrated in combination with IL-12. Page 378, and page 90, Figure 2c. It would therefore have been obvious to one of ordinary skill in the art to have used the combination of IL-12 and IGIF to increase the production of IFN-γ in an animal to help in treating an infection.

Conclusion

23. Claim 19 is objected to as depending from a rejected claim.

24. Claims 1, 2, and 4-9 are found allowable, and claims 19, and its dependant claims would be allowable if amended so as not to depend on the rejected subject matter.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
May 14, 2003

JAMES HOUSEL 5/17/03
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